

REMARKS

Claim 1 has been amended to specify that “the graft composition further comprises a glycoprotein.”

Rejection of Claims 1, 2, and 12 Under 35 U.S.C. § 102(b)-

The Examiner has rejected claims 1, 2, and 12 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,399,123 (hereinafter the ‘123 patent). The Examiner contends that the ‘123 patent teaches a method of using basement membrane for the treatment of hernias, which requires the repair of abdominal wall. The Examiner further contends that cellular components are removed from the basement membrane, and that this process would remove DNA and endotoxins as well. Applicants respectfully traverse the Examiner’s rejection. The ‘123 patent does not anticipate claims 1, 2, and 12 of the instant application.

Anticipation exists only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Claims 1, 2 and 12 require an element that is *not* present in the ‘123 patent. Specifically, the claims require the step of “removing endogenous cells, DNA, and endotoxins from the graft composition.”

The ‘123 patent does not teach a method of removing DNA from a graft composition as recited in claims 1, 2, and 12 of the instant application. Instead, the ‘123 patent states that “fibrous tissue of human or animal origin which is derived from dermis, ligament, tendon, areolar tissue, basement membrane or dura mater, can be purified so that all cellular elements such as sweat glands, sebaceous glands and vascular tissue are removed.” The ‘123 patent goes on to indicate that, prior to the first enzyme treatment, the tissue may be soaked in 0.5-1.9M sodium chloride solution. The step of soaking the fibrous tissue in a 0.5-1.9 M salt

solution should result in hypertonic lysis of cells in the tissue. Lysis of the cells typically results in release of material from the cells and contamination of the tissue, specifically by DNA. The method described in the '123 patent also comprises the step of treating the fibrous tissue with a proteolytic enzyme to remove proteins and glycoproteins. The method further comprises the step of treating the fibrous tissue with a carbohydrate-splitting enzyme to remove polysaccharides and mucopolysaccharides. None of these steps would necessarily remove DNA from the fibrous tissue. Therefore, the Examiner cannot assume that the method taught by the '123 patent would necessarily remove DNA from the fibrous tissue.

Furthermore, independent claim 1 has been amended to specify that "the graft composition further comprises a glycoprotein." The '123 patent does not teach a graft composition comprising a glycoprotein. In fact, the '123 patent explicitly states that the fibrous tissue preparation is "free of nonfibrous tissue proteins and antigenic polysaccharides, mucopolysaccharides, and glycoproteins" (see the '123 patent, claims 1 and 3, col. 2, lines 9-16, and col. 4, lines 55-62). Thus, '123 patent does not teach each and every element of the claims, and therefore, cannot anticipate claims 1, 2, and 12 of the instant application. Withdrawal of the rejection of claims 1, 2, and 12 under 35 U.S.C. § 102(b) is respectfully requested.

Rejection of Claims 1-16 Under 35 U.S.C. § 103(a)-

The Examiner has rejected claims 1-16 under 35 U.S.C. § 103(a) as being obvious over WO 98/25637 in view of U.S. Patent No. 5,955,110 (hereinafter the '110 patent) and U.S. Patent No. 4,399,123 (hereinafter the '123 patent). The Examiner contends that Badylak et al. teaches the use of a tissue graft composition comprising liver basement membrane of a warm-blooded vertebrate for repair of damaged or diseased tissues, where the composition is treated to remove cells and cellular components. The Examiner further contends that one skilled in the art would have been motivated to use the invention of Badylak et al. for the repair of the abdominal

wall because Patel et al. teaches the use of a multilayered, homolaminate submucosal graft for abdominal wall repair and the '123 patent teaches a method for using basement membrane for the treatment of hernias. Applicant respectfully traverses the Examiner's rejection. Applicant's amended claims 1-16 are not obvious over WO 98/25637 in view of the '110 patent and the '123 patent.

A. All the Claim Limitations Must be Taught or Suggested by the Prior Art-

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Therefore, in order for Applicant's invention to be rendered obvious under 35 U.S.C. § 103, the combination of references relied upon by the Examiner must teach each and every element of Applicant's invention, as defined by claims 1-16. Applicant's claims 1-16 require the step of removing DNA from the graft composition. Because WO 98/25637, the '110 patent, and the '123 patent do not provide any suggestion of the specific element of removing DNA from the graft composition, the references either alone or when combined are incapable of defeating the patentability of Applicant's claims 1-16. Thus, Applicant's claims 1-16 are not obvious over WO 98/25637 in view of the '110 patent and the '123 patent.

B. References Must Be Considered as a Whole, Including Portions That Would Lead Away from the Claimed Invention-

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Here, the '123 patent cited by the Examiner teaches away from amended claims 1-16 of the instant application. Applicant has amended the claims to indicate that "the graft composition further comprises a glycoprotein."

The '123 patent explicitly states that the fibrous tissue preparation is "free of nonfibrous tissue proteins and antigenic polysaccharides, mucopolysaccharides, and glycoproteins" (see the '123 patent: claims 1 and 3; col. 2, lines 9-16; and col. 4, lines 55-62). The '123 patent states that glycoproteins are antigenic and their removal (step 1) is required to create a fibrous tissue composition that is suitable for implantation (see the '123 patent, col. 3, lines 33-59). Because the '123 patent teaches a fibrous tissue free of glycoproteins, the reference cannot suggest a graft composition comprising basement membrane of a warm-blooded vertebrate and further comprising a glycoprotein as specified in amended claims 1-16. Therefore, it is clear that the '123 patent expressly teaches away from Applicant's amended claims 1-16 because the prepared graft composition "further comprises a glycoprotein." Thus, Applicant's claims 1-16 are not obvious over WO 98/25637 in view of the '110 patent and the '123 patent.

C. There is No Teaching, Suggestion, or Motivation to Combine the References-

The Examiner contends that one skilled in the art would have been motivated to use the invention of WO 98/25637 for the repair of the abdominal wall because the '110 patent teaches the use of a multilayered, homolaminate submucosal graft for abdominal wall repair and the '123 patent teaches a method for using basement membrane for the treatment of hernias (see page 7 of the August 20, 2008, Office Action). To support a conclusion of obviousness, there must be some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine the prior art reference teachings to arrive at the claimed invention (see MPEP §2143). Contrary to the Examiner's contention, there is no motivation to combine the teachings of WO 98/25637 with the teachings of the '123 patent. The '123 patent teaches away from its combination with WO 98/25637 because WO 98/25637 discloses a graft composition further comprising glycoproteins. A skilled artisan would not

combine a reference that teaches that glycoproteins must be removed to create a tissue composition that is suitable for implantation, with a reference that teaches the use of a tissue graft composition comprising liver basement membrane with added glycoproteins for the repair of damaged or diseased tissues. Therefore, the '123 patent cited by the Examiner cannot be properly combined with Badylak et al. There is no reason why one skilled in the art would turn from WO 98/25637 to the '123 patent because the '123 patent teaches the avoidance of glycoproteins in tissue compositions suitable for implantation.

Furthermore, a skilled artisan would not have been motivated to combine the teaching of WO 98/25637 and the '110 patent with a reasonable expectation of success. Applicant's claims 1-16 specify the repair of body wall tissue that comprises a multilaminate, stratified structure comprising a combination of differentiated tissue types, including connective tissue, skeletal muscle, adipose tissue, epidermal tissue, and the serous lining of the body wall cavity. Consequently, because of the complexity of body wall tissue, a skilled artisan would not have had a reasonable expectation of success to substitute liver basement membrane for the intestinal tissue-derived graft compositions described in the '110 patent to repair body wall tissue.

The '110 patent describes graft compositions comprising intestinal submucosa tissue, and discloses the use of those graft compositions for the repair of hernias and gastroschisis. WO 98/25637 describes graft compositions comprising liver basement membrane. The graft compositions described in WO 98/25637 are not compositionally and structurally identical to those described in the '110 patent. Accordingly, it is not obvious that the liver-derived graft compositions described in WO 98/25637 could be substituted for the compositions described in the '110 patent. Nor would a skilled artisan, at the time the present application was filed, have had a reasonable expectation of success in substituting the graft compositions of WO 98/25637 comprising liver basement membrane for the compositions described in the '110 patent

to effectively repair *in vivo* a complex structure such as a multilaminate, stratified structure comprising differentiated tissue types including connective tissue, skeletal muscle, adipose tissue, epidermal tissue, and the serous lining of the body wall cavity.

Moreover, Applicant's statements, cited by the Examiner, that liver basement membrane tissue "can be substituted for intestinal submucosa tissue in most, if not all, of the applications previously reported for intestinal submucosa, including enhancing wound healing, promoting endogenous tissue growth, stimulating cell proliferation and inducing cell differentiation" refer generally to effects of liver basement membrane graft compositions, not to the specific effect of repair of body wall. Contrary to the Examiner's contention, these statements do not render Applicant's claims 1-16 obvious. Again, as noted in our last response, these statements do not indicate that liver basement membrane would be effective in repairing *in vivo* a complex, multilaminate, stratified structure comprising multiple differentiated tissue types including connective tissue, skeletal muscle, adipose tissue, epidermal tissue, and the serous lining of the body wall cavity.

Thus, contrary to the Examiner's contention, claims 1-16 of the instant application are not obvious over WO 98/25637 in view of the '110 patent and the '123 patent. Withdrawal of the rejection of claims 1-16 under 35 U.S.C. § 103(a) as being obvious over WO 98/25637 in view of the '110 patent and the '123 patent is respectfully requested.

Rejection of Claims 1-16 For Obviousness-Type Double Patenting-

The Examiner has rejected claims 1-16 as being unpatentable for obviousness-type double patenting over claims 1-3 and 9 of U.S. Patent No. 6,793,939 (hereinafter the '939 patent) in view of the '110 patent, WO 98/25637, and the '123 patent. The '939 patent is a

continuation application of the U.S. national application that was based on the PCT application that published as WO 98/25637. Applicant respectfully traverses the Examiner's rejection.

Claims 1, 3 and 9 of the '939 patent are directed to tissue graft compositions comprising liver basement membrane wherein the basement membrane is devoid of endogenous cells. The claims do not require that DNA and endotoxins be removed from the graft composition. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Therefore, in order for Applicant's invention to be rendered unpatentable for obviousness-type double patenting, the combination of references relied upon by the Examiner must teach each and every element of Applicant's invention, as defined by claims 1-16. Applicant's claims 1-16 require the step of removing DNA from the graft composition. Because claims 1, 3 and 9 of the '939 patent, WO 98/25637, the '110 patent, and the '123 patent do not provide any suggestion of the specific element of removing DNA from the graft composition, the references either alone or when combined are incapable of defeating the patentability of Applicant's claims 1-16.

Furthermore, because the claims of the instant application require that the graft composition comprise a glycoprotein, the teaching away argument with respect to the '123 patent, and the motivation argument with respect to WO 98/25637 in combination with the '110 patent and the '123 patent, apply with equal force to this obviousness-type double patenting rejection. Therefore, amended claims 1-16 are not obvious over claims 1-3 and 9 of the '939 patent in view of the '110 patent, WO 98/25637, and the '123 patent. Withdrawal of the rejection of claims 1-16 for obviousness-type double patenting is respectfully requested.

Provisional Rejection of Claims 1-16 For Obviousness-Type Double Patenting-

The Examiner has provisionally rejected claims 1-16 as being unpatentable for obviousness-type double patenting over claims 24 and 25 of co-pending application number 10/775,386 in view of the '110 patent, WO 98/25637, and the '123 patent. Application number 10/775,386 (hereinafter the '386 application) is a continuation application of the U.S. national application that was based on the PCT application that published as WO 98/25637. Applicant respectfully traverses the Examiner's rejection.

Claims 24 and 25 of the '386 application are directed to tissue graft compositions comprising gelled liver basement membrane, wherein the basement membrane is substantially free of endogenous cells. The claims do not require that DNA and endotoxins be removed from the graft composition. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Therefore, in order for Applicant's invention to be rendered unpatentable for obviousness-type double patenting, the combination of references relied upon by the Examiner must teach each and every element of Applicant's invention, as defined by claims 1-16. Applicant's claims 1-16 require the step of removing DNA from the graft composition. Because claims 24 and 25 of the '386 application, WO 98/25637, the '110 patent, and the '123 patent do not provide any suggestion of the specific element of removing DNA from the graft composition, the references either alone or when combined are incapable of defeating the patentability of Applicant's claims 1-16.

Furthermore, because the claims of the instant application require that the graft composition comprise a glycoprotein, the teaching away argument with respect to the '123 patent, and the motivation argument with respect to WO 98/25637 in combination with the '110 patent and the '123 patent, apply with equal force to this provisional obviousness-type double patenting rejection. Therefore, amended claims 1-16 are not obvious over claims 24 and 25 of

the '386 application in view of the '110 patent, WO 98/25637, and the '123 patent. Withdrawal of the provisional rejection of claims 1-16 for obviousness-type double patenting is respectfully requested.

CONCLUSION

The foregoing amendments and remarks are believed to fully respond to the Examiner's rejections. The claims are believed to be in condition for allowance. Applicant respectfully requests allowance of the claims, and passage of the application to issuance.

Respectfully submitted,

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